REMARKS

Claims 112-183 are presented for examination. Claims 12, 14, 15, 17, 20-23, 25, 26, 38, 40-42, 44, 47-50, 52-103 and 108-111 are withdrawn, without prejudice or disclaimer. Claims 1-11, 13, 16, 18, 19, 24, 27-37, 39, 43, 45, 46, 51 and 104-107 are cancelled, without prejudice or disclaimer.

The February 23, 2009 Office Action rejected claims 1, 2, 4, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. It is noted that claims 1, 2, 4, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 have hereby been cancelled, without prejudice or disclaimer. Thus, the rejections of claims 1, 2, 4, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §112, first paragraph, is moot and should be withdrawn.

The February 23, 2009 Office Action rejected claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27-28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a) as allegedly being unpatentable over WO 98/12243, hereinafter "Jarrett et al." in view of Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous bone lumbar spinal fusion, hereinafter "Helm et al." or The use of Demineralized Bone Matrix in the Repair of Segmental Defects, hereinafter "Bolander et al." It is noted that claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27-28, 31-37, 39, 43, 45, 46, 51 and 104-107 have hereby been cancelled, without prejudice or disclaimer. Thus, the rejections of claims 1, 2, 5-11, 13, 16, 18, 19, 24, 27-28, 31-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a), is moot and should be withdrawn.

The February 23, 2009 Office Action rejected claims 1, 2, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a) as allegedly being unpatentable over Jarrett et al. in view of Helm et al. or Bolander et al., and further in view of Optimizing Human Demineralized Bone Matrix for Clinical Application, hereinafter "Maddox et al." It is noted that claims 1, 2, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 have hereby been cancelled, without prejudice or disclaimer. Thus, the rejections of claims 1, 2, 4-11, 13, 16, 18, 19, 24, 27, 28, 30-37, 39, 43, 45, 46, 51 and 104-107 under 35 U.S.C. §103(a), is moot and should be withdrawn.

In an effort to expedite prosecution of the present application, Applicants will show how the currently claimed invention as a whole would not have been obvious to a person having ordinary skill in the art at the time the invention was made, as required by 35 U.S.C. §103.

Included with this Amendment and Response (attached as Appendix A) is a declaration under 37 C.F.R. § 1.132 ("The Lin Declaration"), which has been signed by one of the inventors of the present application. The declaration establishes that inventor Dr. Steve T. Lin (whose curriculum vitae is enclosed as Exhibit A) disagrees with the Office Action combining the teachings of the section entitled "Application for the Macromers. Method of Treatment" at pages 24-26 of Jarrett et al., with the teachings of another totally unrelated section entitled "Controlled delivery of incorporated agents" at pages 27-28 of Jarrett et al., to come up with the claimed invention because sealing a leak in a bone is not related to controlled delivery of an agent to a tissue surface to treat a localized medical condition. Consequently, a person of ordinary skill in the art reading Jarrett et al., including the totally unrelated passages cited above, would NOT have been motivated to consider using a Jarrett et al. carrier composition comprising osteotherapeutic material(s) to promote the formation of new bone (see The Lin Declaration at Para. 19). Similarly, it is Dr. Steve T. Lin's opinion that the specific selection of the species Demineralized Bone Matrix for the large genus of "bone graft substitutes" is hindsight. Even if a person of ordinary skill in the art would have been motivated to take a broad interpretation of the teachings of the Jarrett et al. reference of "[i]n orthopedic surgery, uses include tendon repair, bone repair, including filling of defects, and meniscus repair" to include promoting the formation of new bone using a composition comprising an osteotherapeutic bone graft substitute material, which in no way is conceded to, the size of the prior art genus of "bone graft substitute" is so large that a person of ordinary skill in the art would NOT have been motivated to specifically select the species Demineralized Bone Matrix, over any of the other species of the bone graft substitute genus (see The Lin Declaration at Para. 25).

Applicants note that according to MPEP 2144.08, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. A proper obviousness analysis involves: determining the scope and contents of the prior art; ascertaining the differences between the prior art and claims in issue; determining the level of ordinary skill in the pertinent art; and evaluating any evidence of secondary considerations.

The Office Action first cites to Jarrett et al. at page 25, lines 11 and 12, for support for use of the Jarrett et al. carrier composition in orthopedic surgery, as bone repair. The cited material is written in the sub-section entitled "Sealing Leaks in Tissue" which is part of the general section entitled "Application for the Macromers. Method of Treatment". The general section states that "[g]enerally, any medical condition which requires a coating or sealing layer may be treated by the

methods described herein to produce a coating with better adherence"; and the sub-section states that "[i]n orthopedic surgery, uses include tendon repair, bone repair, including filling of defects, and meniscus repair" (see The Lin Declaration at Para. 15). Based on these sections, a person of ordinary skill in the art would be motivated to use a Jarrett et al. carrier composition for sealing a leak in a bone, e.g., for repairing a bone defect with a leak such as a cerebrospinal fluid (CSF) leak. In fact, the examples found in Jarrett et al. support this teaching of using a Jarrett et al. carrier composition for sealing a leak in a bone. Example 5, at pages 41-42 of Jarrett et al., describe "Sealing of Dural Leak in Canine Craniotomy" (see The Lin Declaration at Para. 16).

The Office Action then cites to Jarrett et al. at page 27, line 2 to page 28, line 13, for support for use of the Jarrett et al. carrier composition as a drug delivery device for the delivery of therapeutic agents. The cited material is written in the section entitled "Controlled delivery of incorporated agents". This section states that "[a]nother preferred application involves locally applying an incorporated agent, such as a prophylactic, therapeutic or diagnostic agent, to tissue surfaces of a patient. The method includes the steps of mixing an agent to be incorporated with an aqueous solution including a suitable polymerization initiator, such as a light-sensitive free-radical polymerization initiator, and a macromer, to form a coating mixture. Tissue surfaces are coated with the coating mixture and the macromer is polymerized, for example, by exposure of the coating mixture to an effective amount of light of an appropriate wavelength" (see The Lin Declaration at Para. 17). Based on this totally unrelated section, a person of ordinary skill in the art would be motivated to consider using a Jarrett et al. carrier composition for the controlled delivery of an agent to a tissue surface to treat a localized medical condition (see The Lin Declaration at Para. 18).

A person of ordinary skill in the art reading these two unrelated sections, however, would NOT be motivated to combine the teachings of the section entitled "Application for the Macromers. Method of Treatment" at pages 24-26 of Jarrett et al., with the teachings of another totally unrelated section entitled "Controlled delivery of incorporated agents" at pages 27-28 of Jarrett et al., to come up with the claimed invention because sealing a leak in a bone is not related to controlled delivery of an agent to a tissue surface to treat a localized medical condition (see The Lin Declaration at Para. 19).

In *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1537, 218 USPQ 871, 877 (Fed. Cir. 1983), the Court noted that "the question under 35 U.S.C. § 103 is not whether the differences

[between the claimed invention and the prior art] would have been obvious" but "whether the claimed invention *as a whole* would have been obvious."

Applicants respectfully submit that given the teaching of Jarrett et al., the claimed invention as a whole (i.e., a composition comprising demineralized bone matrix in a hydrogel carrier) would not have been obvious. The Office Action acknowledges (at page 5 of the February 23, 2009 Office Action) that "[w]hile Jarrett discloses the carrier composition of the claimed invention, and while Jarrett discloses that the carrier composition is a drug delivery device and specifically mentions the use of the composition for repair of bone, the carrier composition of Jarrett does not contain demineralized bone matrix material. However, it is known in the art that demineralized bone matrix is used for bone repair according to Helm and Bolander. Therefore, taking the general teachings of the prior art, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that inclusion of demineralized bone matrix in the composition of Jarrett would effectively repair bone" (see The Lin Declaration at Para. 20). Applicants respectfully disagree.

Several categories of bone graft substitutes exist and encompass a variety of materials, material sources, and origins (natural vs synthetic). Many are formed from composites of 1 or more types of material. Consequently, the existence of numerous categories of bone graft substitutes, each encompassing a variety of materials, material sources, and origins, highlights the fact that the bone graft substitute genus includes a substantially large number of species (see The Lin Declaration at Para. 21).

Dr. Steve T. Lin performed a search on the "PubMed" database on or about December 4, 2008 using the keywords "Bone Graft Substitutes". A printout of the search results is attached as Exhibit B. As seen from this Exhibit B, the keywords "Bone Graft Substitutes" returned **1,902 citations**. Of these 1,902 citations, only 147 included the keywords "Demineralized Bone Matrix (DBM)". The bulk of the citations (i.e., **over 1700 citations**) were related to citations directed to **other** species of bone graft substitutes. Given such a large number of species available in the bone graft substitute genus, a person of ordinary skill in the art would not be motivated to specifically select the species of Demineralized Bone Matrix, over any of the other species encompassing the bone graft substitute genus (see The Lin Declaration at Para. 22).

The Jarrett et al. reference does not expressly teach a particular reason to select the specific species of Demineralized Bone Matrix, especially since there is NO teaching or suggestion in Jarrett et al. of a composition comprising the Jarrett et al. carrier composition and a bone graft substitute material to promote the formation of new bone. Given NO express teaching or particular reason as to why a person of ordinary skill in the art should select the specific species of Demineralized Bone Matrix, a person of ordinary skill in the art would NOT have been motivated to choose the specific species of Demineralized Bone Matrix over any of the other species encompassing the bone graft substitute genus (see The Lin Declaration at Para. 23).

The Jarrett et al. reference also does not teach a "typical", "preferred," or "optimum" "incorporated agent, such as a prophylactic, therapeutic or diagnostic agent" to promote the formation of new bone. As described above, several categories of bone graft substitutes exist and encompass a variety of materials, material sources, and origins (natural vs synthetic). Many bone graft substitutes are formed from composites of 1 or more types of material. Considering the number of variables which must be selected or modified, and the nature and significance of the differences between the large number of bone graft substitute materials, a person of ordinary skill in the art would NOT have been motivated to specifically choose the species Demineralized Bone Matrix over any of the other species encompassing the bone graft substitute genus (see The Lin Declaration at Para. 24).

Based on the above, the specific selection of the species Demineralized Bone Matrix for the large genus of "bone graft substitutes" is hindsight. Even if a person of ordinary skill in the art would have been motivated to take a broad interpretation of the teachings of the Jarrett et al. reference of "[i]n orthopedic surgery, uses include tendon repair, bone repair, including filling of defects, and meniscus repair" to include promoting the formation of new bone using a composition comprising an osteotherapeutic bone graft substitute material, which in no way is conceded to, the size of the prior art genus of "bone graft substitute" is so large that a person of ordinary skill in the art would NOT have been motivated to specifically select the species Demineralized Bone Matrix, over any of the other species of the bone graft substitute genus (see The Lin Declaration at Para. 25).

Therefore, it is respectfully submitted that pending claims 112-183 are in condition for allowance. Support for new claims 112-183 are found throughout Applicants as-filed application, including the original claims and figures, and this, no new matter has been added.

Accordingly, it is respectfully submitted that each rejection raised in the February 23, 2009 Office Action has been overcome and that the above-identified application is now in condition for allowance. For this reason, the Amendment should be entered.

The Commissioner for Patents is hereby authorized to charge any fees associated with the filing of this Amendment and RCE, including the three-month extension of time fee, to Deposit Account No. 50-1561, Reference 019870-052201/US.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,
GREENBERG TRAURIG, LLP

Dated: January 25, 2010

By: /Barry J. Schindler/
Barry J. Schindler
Registration No. 32,938

Mailing Address:
GREENBERG TRAURIG, LLP
MetLife Building
200 Park Avenue
New York, NY 10166
Telephone: (212) 801-2100
Facsimile: (212) 801-6400